Remarks

Claims 1and 6 are here amended and new claims 29-32 are here added. Support for amendment of claim 1 is found in this claim as originally filed and in the specification of PCT application PCT/US04/40660 and in corresponding U.S. patent application 2007/0259008 as originally filed as follows:

claim 1 line 2: the PCT specification page 18, ¶[0071] line 24 (U.S. patent application page 10, ¶[0016] lines 2-3);

claim 1 lines 4-5: the PCT specification page 18, ¶[0071] line 24 (U.S. patent application page 10, ¶[0016] lines 2-3); and

claim 1 line 10: the PCT specification page 2, ¶[0009] line 26 (U.S. patent application page 1, ¶[009] lines 3 and 5-6) and page 8, ¶[0043] lines 32-33 (U.S patent application page 5, ¶[0087] lines 8-9).

Support for amendment of claim 6 is found in this claim as originally filed and in the PCT specification page 18, ¶[0071] line 24 (U.S. patent application page 10, ¶[0016] lines 2-3).

Support for new claim 29 is found in claims 1 and 18 as originally filed and in the PCT specification page 9, ¶[0043] line 13 (U.S. patent application page 5, ¶[0087] line 36).

Support for new claim 30 is found in the PCT specification page 4, ¶[0013] lines 4-5 (U.S. patent application page 2 ¶[0034] line 8).

Support for new claim 31 is found in claims 1, 4, 9-10, 13 and 20-22 as originally filed and in the PCT specification page 2, ¶[0009] line 28 (U.S. patent application page 1, ¶[0009] line 7) and Figures 7 and 8.

Support for new claim 32 is found in claims 1, 4, 7-13 and 18-22 as originally filed and in the PCT specification page 4, ¶[0014] lines 9-10 (U.S. patent application page 2, ¶[0035] lines 1-4) and Figures 7 and 8.

Upon entry of the present Amendment and Response claims 1-13, 18-23 and 29-32 are pending. No new matter has been added, and no matter presented that would necessitate an additional search on the part of the Examiner. Applicants reserve the right to prosecute subject matter of claims as originally filed in this application or in another application having the same filing date and/or priority date as present application.

Applicants acknowledge with appreciation withdrawal by the Office action of rejection of claims 1 and 18-20 under 35 U.S.C. §102(a) in view of Bulmus et al., 2003 J Controlled Release 93:105.

Applicants acknowledge with appreciation withdrawal by the Office action of the rejection under 35 U.S.C. §103(a) of:

claims 1-13 and 20 in view of LaFleur et al., U.S. patent number 6,472,512 and Cammas et al., 1999 Int J Biol Macromol 25:273, and in further view of Saito et al., 2003 Adv Drug Del Rev 55:199;

claims 1-13 and 18-20 in view of LaFleur et al., U.S. patent number 6,472,512 and Cammas et al., 1999 Int J Biol Macromol 25:273, and in further view of Summerton et al., 1997 Nuc Acid Drug Dev 7:187; and

claims 1-13 and 20-23 in view of LaFleur et al., U.S. patent number 6,472,512 and Cammas et al., 1999 Int J Biol Macromol 25:273, and in further view of Khazenzon et al., 2003 Mol Cancer Ther 2:985.

Applicants believe that a brief description of independent claim 1 as here amended would be helpful to the reader prior to addressing issues in the Office action.

Claim 1 as here amended is directed to a drug delivery molecule having: a polymerized carboxylic acid molecular scaffold with a plurality of pendant carboxylic acid groups, a plurality of biologically active molecular modules, such that each module is covalently linked to a pendant carboxylic acid of the molecular scaffold, and the active modules having: at least one targeting module for promoting cellular uptake by a target cell, and at least one pro-drug module for altering cellular metabolism of the target cell, such that the targeting or the pro-drug active module includes a polypeptide and/or polynucleotide, such that the scaffold includes a polymalic acid or a polymalate derivative.

Claims are novel

The Office action page 5 ¶15 rejects claims 1-2, 6-13 and 18-23 under 35 U.S.C. §102(b) in view of Lee et al., Proceedings of the American Association for Cancer Research Annual Meeting, March 2004 vol. 45: pages 149-150. Applicants respectfully traverse the rejection for the reasons below.

The Manual of Patent Examining Procedure asserts that Applicant's disclosure of his or her own work within the year before the application filing date cannot be used against him or her under 35 U.S.C.§102(a). M.P.E.P. §2132.01 citing *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982).

Further, 35 U.S.C. §102(b) states that a person shall be entitled to a patent unless the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.

Lee et al. cited in the Office action was published as an abstract in the proceedings of a meeting March 2004. This date is within one year, the grace period of the filing date of the present application December 3, 2004.

Further, the pending claims as here amended have the benefit of provisional application 60/527,300 filed December 5, 2003, prior to publication of Lee et al.

For any of these reasons claims 1-2, 6-13 and 18-23 as here amended comply with 35 U.S.C. §102(b). Applicants respectfully assert that rejection of these claims can be properly withdrawn.

Claims as here amended comply with 35 U.S.C. §112 ¶1

The Office action page 3 ¶ 6 rejects claims 1-2, 6-13 and 18-23 under 35 U.S.C. §112 ¶1, new matter. Applicants here amend claim 1 in response to the comments in the Office action. Claims 1 as here amended is directed to a molecule that includes "a polymalic acid or a polymalate derivative." The term "homopolymer" has been deleted. Accordingly, claim 1 as here amended complies with 35 U.S.C. §112 ¶1.

According to the Manual of Patent Examining Procedure, the test for sufficiency of the written description is whether the disclosure of the application relied upon, reasonably conveys to the skilled artisan that the inventor had possession of the invention as of filing date. M.P.E.P. §2164.02.

Factual analysis of the Applicants specification as originally filed supports the term "polymalic acid." The specification of the PCT application PCT/US04/40660 is replete with examples of polymalic acid based molecules and includes sections pages 8 and 18 entitled "Synthesis of a polymalic acid based multifunctional carrier system for the tumor targeted

delivery of morpholino antisense oligonucleotides" and "Treatment of human glioblastoma grown in brain of nude rat with laminin-8 antisense oligonucleotides conjugated to poly-L-malic acid."

Factual analysis of the Applicants' specification as originally filed shows also ample support for the term "polymalate derivative." For example, the specification of PCT application page 8, ¶[0043] lines 33-34 describes certain polymalate derivatives and block polymers.

Therefore, the description of the subject matter of claim 1 as here amended is fully supported by the specification as originally filed. This description would have conveyed to the skilled artisan at the time application was filed that Applicants were in possession of the subject matter of the claim 1 as here amended.

Applicants assert that claim 1 as here amended satisfies the written description requirement.

Applicants respectfully assert that rejection under 35 U.S.C. §112 ¶1 of claims 1-2, 6-13 and 18-23 as here amended can properly be withdrawn.

Claims as here amended have the benefit of provisional application 60/527,300

The Office action pages 2-3 ¶4 states that independent claim 1 and claims dependent from claim 1 of this patent application, filed December 3, 2004 as PCT application PCT/US04/40660, are broader than the subject matter in the provisional application 60/527,300 filed December 5, 2003. The word "homopolymer" is deleted from claim 1 as here amended.

The Office action page 2 ¶4 lines 8-9 to page 3 lines 1-3 admits that the provisional application shows polymalic acid with molecular modules attached to the pending carboxyl groups and alleges that the previous listing of the claims did not require direct attachment to the pending carboxyl groups.

Applicants here further amend claims 1 and 6 to add the word "pendant" to describe carboxyl groups. Claim 1 as amended is directed to a drug delivery molecule including a polymerized carboxylic acid molecular scaffold having a plurality of pendant carboxylic acid groups, a plurality of biologically active molecular modules, such that each module is covalently linked to a pendant carboxylic acid of the molecular scaffold.

Applicants assert that the term "pendant" is preferable to "pending" in conjunction with the words "carboxylic acid groups" because "pendant" is supported by the specification of the

PCT application and was used interchangeably with "pending" by Applicants in the PCT and provisional applications. The terms were used to describe carboxylic groups that as drawn in chemical formulae, appeared to be suspended or hanging from the polymeric backbone, and the site of covalently attached biologically active, i.e., functional modules. The words share the root "pend" according to The American Heritage Dictionary of the English Language, ed. William Morris, published Houghton Mifflin Co. 1979. Support for the term "pendant" is found in the PCT specification as originally filed as follows:

> Polymalic acid (PMLA). A multifunctional drug delivery construct consists of modules attached to the pendant carboxyl groups of polymalic acid (PMLA). The polymer is a natural product of *Physarum polycephalum* [27]. The modules are (1) morpholino antisense oligonucleotides conjugated to the scaffold by disulfide bonds, which bonds are cleaved in the cytoplasm to release the free drug, (2) antibodies against transferrin receptor for cancer cell targeting and receptor-mediated endocytosis, (3) short chain PEG-conjugated L-leucine and directly coupled L-valine, both linked through amide bonds, to provide pH-dependent lipophilicity to disrupt endosomal membranes, (4) long chain PEG for increasing time in circulation, and (5) fluorescent reporter molecules (fluorescein, Cy5 or similar fluorophores) to detect the construct molecule within the tissue/cell [Ibid., page 18 ¶[0071] emphasis added].

The facts of the provisional application show almost identical description of the drug delivery molecule that is the subject matter of claim 1 as here amended other than use of "pending" rather than "pendant." See Provisional patent application 60/527,300 page 1 ¶3. Therefore, the subject matter of claim 1 as here amended is supported by the provisional application. Claims 2, 6-13 and 18-23 depend directly or indirectly from claim 1 and include all of the subject matter of claim 1 as here amended, and are likewise so amended.

For at least this reason claims as here amended have the benefit of provisional application 60/527,300.

Summary

On the basis of the foregoing amendments and reasons, Applicants respectfully submit that the pending claims are in condition for allowance, which is respectfully requested. As this response is filed within two months of mailing of the Office action, Applicants respectfully request an Advisory Action.

In the event that the Examiner determines that other matters require attention before allowance, the Examiner is respectfully requested and encouraged to contact Applicants' representative at the telephone number provided.

Respectfully submitted,

Marina Sigarova
Registration number 64,233
Sonia K. Guterman
Registration number 44,729
Lawson & Weitzen, LLP
88 Black Falcon Ave., Suite 345
Boston MA 02210-2481
Tel: (617) 439-4990
Fax: (617) 439-3987
Customer Number 48425

Dated: January 28, 2011